NLE的AMBER FF19SB参数拟合

拟合前参数准备

检查配套的力场参数（leaprc.protein.ff19SB）

addAtomTypes

addPdbResMap

```
#       Load the main parameter set.
#
set default cmap on
parm19 = loadamberparams parm19.dat
frcmod19SB = loadamberparams frcmod.ff19SB
#
#       Load main chain and terminating amino acid libraries
#
loadOff amino19.lib
loadOff aminoct12.lib
loadOff aminont12.lib
```

注意后续原子的命名和其他参照信息都需要与**parm19.dat**保持一致

查看相近标准氨基酸的RESP参数

该参数可与拟合后的NLE参数进行对比

amino19.lib

```
!entry.ALA.unit.atoms table  str name  str type  int typex  int resx  int flags  int seq  int elmnt  dbl chg
 "N" "N" 0 1 131072 1 7 -0.415700
 "H" "H" 0 1 131072 2 1 0.271900
 "CA" "XC" 0 1 131072 3 6 0.033700
 "HA" "H1" 0 1 131072 4 1 0.082300
```

```
 "CB" "CT" 0 1 131072 5 6 -0.182500
 "HB1" "HC" 0 1 131072 6 1 0.060300
 "HB2" "HC" 0 1 131072 7 1 0.060300
 "HB3" "HC" 0 1 131072 8 1 0.060300
 "C" "C" 0 1 131072 9 6 0.597300
 "O" "O" 0 1 131072 10 8 -0.567900

 !entry.ILE.unit.atoms table  str name  str type  int typex  int resx  int flags  int seq  int elmnt  dbl chg
 "N" "N" 0 1 131072 1 7 -0.415700
 "H" "H" 0 1 131072 2 1 0.271900
 "CA" "XC" 0 1 131072 3 6 -0.059700
 "HA" "H1" 0 1 131072 4 1 0.086900
 "CB" "3C" 0 1 131072 5 6 0.130300
 "HB" "HC" 0 1 131072 6 1 0.018700
 "CG2" "CT" 0 1 131072 7 6 -0.320400
 "HG21" "HC" 0 1 131072 8 1 0.088200
 "HG22" "HC" 0 1 131072 9 1 0.088200
 "HG23" "HC" 0 1 131072 10 1 0.088200
 "CG1" "2C" 0 1 131072 11 6 -0.043000
 "HG12" "HC" 0 1 131072 12 1 0.023600
 "HG13" "HC" 0 1 131072 13 1 0.023600
 "CD1" "CT" 0 1 131072 14 6 -0.066000
 "HD11" "HC" 0 1 131072 15 1 0.018600
 "HD12" "HC" 0 1 131072 16 1 0.018600
 "HD13" "HC" 0 1 131072 17 1 0.018600
 "C" "C" 0 1 131072 18 6 0.597300
 "O" "O" 0 1 131072 19 8 -0.567900


 !entry.LEU.unit.atoms table  str name  str type  int typex  int resx  int flags  int seq  int elmnt  dbl chg
 "N" "N" 0 1 131072 1 7 -0.415700
 "H" "H" 0 1 131072 2 1 0.271900
 "CA" "XC" 0 1 131072 3 6 -0.051800
 "HA" "H1" 0 1 131072 4 1 0.092200
 "CB" "2C" 0 1 131072 5 6 -0.110200
 "HB2" "HC" 0 1 131072 6 1 0.045700
 "HB3" "HC" 0 1 131072 7 1 0.045700
 "CG" "3C" 0 1 131072 8 6 0.353100
```

```
 "HG" "HC" 0 1 131072 9 1 -0.036100
 "CD1" "CT" 0 1 131072 10 6 -0.412100
 "HD11" "HC" 0 1 131072 11 1 0.100000
 "HD12" "HC" 0 1 131072 12 1 0.100000
 "HD13" "HC" 0 1 131072 13 1 0.100000
 "CD2" "CT" 0 1 131072 14 6 -0.412100
 "HD21" "HC" 0 1 131072 15 1 0.100000
 "HD22" "HC" 0 1 131072 16 1 0.100000
 "HD23" "HC" 0 1 131072 17 1 0.100000
 "C" "C" 0 1 131072 18 6 0.597300
 "O" "O" 0 1 131072 19 8 -0.567900


 !entry.VAL.unit.atoms table  str name  str type  int typex  int resx  int flags  int seq  int elmnt  dbl chg
 "N" "N" 0 1 131072 1 7 -0.415700
 "H" "H" 0 1 131072 2 1 0.271900
 "CA" "XC" 0 1 131072 3 6 -0.087500
 "HA" "H1" 0 1 131072 4 1 0.096900
 "CB" "3C" 0 1 131072 5 6 0.298500
 "HB" "HC" 0 1 131072 6 1 -0.029700
 "CG1" "CT" 0 1 131072 7 6 -0.319200
 "HG11" "HC" 0 1 131072 8 1 0.079100
 "HG12" "HC" 0 1 131072 9 1 0.079100
 "HG13" "HC" 0 1 131072 10 1 0.079100
 "CG2" "CT" 0 1 131072 11 6 -0.319200
 "HG21" "HC" 0 1 131072 12 1 0.079100
 "HG22" "HC" 0 1 131072 13 1 0.079100
 "HG23" "HC" 0 1 131072 14 1 0.079100
 "C" "C" 0 1 131072 15 6 0.597300
 "O" "O" 0 1 131072 16 8 -0.567900

 !entry.MET.unit.atoms table  str name  str type  int typex  int resx  int flags  int seq  int elmnt  dbl chg
 "N" "N" 0 1 131072 1 7 -0.415700
 "H" "H" 0 1 131072 2 1 0.271900
 "CA" "XC" 0 1 131072 3 6 -0.023700
 "HA" "H1" 0 1 131072 4 1 0.088000
 "CB" "2C" 0 1 131072 5 6 0.034200
 "HB2" "HC" 0 1 131072 6 1 0.024100
```

```
"HB3" "HC" 0 1 131072 7 1 0.024100
"CG" "2C" 0 1 131072 8 6 0.001800
"HG2" "H1" 0 1 131072 9 1 0.044000
"HG3" "H1" 0 1 131072 10 1 0.044000
"SD" "S" 0 1 131072 11 16 -0.273700
"CE" "CT" 0 1 131072 12 6 -0.053600
"HE1" "H1" 0 1 131072 13 1 0.068400
"HE2" "H1" 0 1 131072 14 1 0.068400
"HE3" "H1" 0 1 131072 15 1 0.068400
"C" "C" 0 1 131072 16 6 0.597300
"O" "O" 0 1 131072 17 8 -0.567900
```

amino19ipq_0.9_vac.lib

```
!entry.NLE.unit.atoms table  str name  str type  int typex  int resx  int flags  int
seq  int elmnt  dbl chg
    "N"     "N"     0   1   131072   1   7 -0.48196
    "H"     "H"     0   1   131072   2   1  0.28343
    "CA"    "CX"    0   1   131072   3   6  0.09488
    "HA"    "H1"    0   1   131072   4   1  0.05160
    "CB"    "2C"    0   1   131072   5   6 -0.10743
    "HB2"   "HC"    0   1   131072   6   1  0.03336
    "HB3"   "HC"    0   1   131072   7   1  0.03336
    "CG"    "2C"    0   1   131072   8   6  0.02915
    "HG2"   "HC"    0   1   131072   9   1  0.00789
    "HG3"   "HC"    0   1   131072  10   1  0.00789
    "CD"    "2C"    0   1   131072  11   6  0.14380
    "HD2"   "HC"    0   1   131072  12   1 -0.00884
    "HD3"   "HC"    0   1   131072  13   1 -0.00884
    "CE"    "CT"    0   1   131072  14   6 -0.31100
    "HE1"   "HC"    0   1   131072  15   1  0.07016
    "HE2"   "HC"    0   1   131072  16   1  0.07016
    "HE3"   "HC"    0   1   131072  17   1  0.07016
    "C"     "C"     0   1   131072  18   6  0.53987
    "O"     "OD"    0   1   131072  19   8 -0.51764
```

aminoct19ipq_0.9.lib

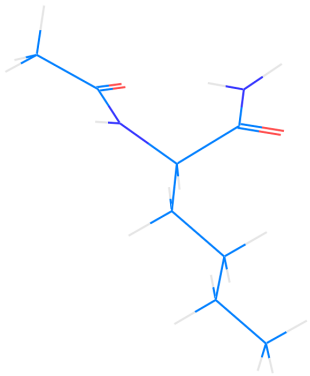
```
!entry.CNLE.unit.atoms table  str name  str type  int typex  int resx  int flags  int seq  int elmnt  dbl chg
    "N"     "N"     0   1   131072   1   7 -0.79156
    "H"     "H"     0   1   131072   2   1  0.37225
    "CA"    "CX"    0   1   131072   3   6  0.36333
    "HA"    "H1"    0   1   131072   4   1 -0.01954
    "CB"    "2C"    0   1   131072   5   6 -0.19327
    "HB2"   "HC"    0   1   131072   6   1  0.04488
    "HB3"   "HC"    0   1   131072   7   1  0.04488
    "CG"    "2C"    0   1   131072   8   6  0.05001
    "HG2"   "HC"    0   1   131072   9   1 -0.00110
    "HG3"   "HC"    0   1   131072  10   1 -0.00110
    "CD"    "2C"    0   1   131072  11   6  0.21636
    "HD2"   "HC"    0   1   131072  12   1 -0.03596
    "HD3"   "HC"    0   1   131072  13   1 -0.03596
    "CE"    "CT"    0   1   131072  14   6 -0.36969
    "HE1"   "HC"    0   1   131072  15   1  0.07735
    "HE2"   "HC"    0   1   131072  16   1  0.07735
    "HE3"   "HC"    0   1   131072  17   1  0.07735
    "C"     "CO"    0   1   131072  18   6  0.82556
    "O"     "O3"    0   1   131072  19   8 -0.85057
    "OXT"   "O3"    0   1   131072  20   8 -0.85057
```

Gaussian优化NLE结构

对NLE进行封端 ACE、NH2

nle.mol2

3.07KB



结构优化

```
antechamber -i NLE.mol2 -fi mol2 -o NLE.gjf -fo gcrt -at amber -gn "%nproc=8" -gm "%mem=4GB"
-gk "#B3LYP/6-311G* opt pop=MK iop(6/33=2,6/42=6)" -rn NLE -ch NLE -nc 0
```

RESP拟合

初步拟合：从gaussian的log文件提取信息

```
antechamber -fi gout -i ../Nle.log -fo ac -o NLE.ac -c resp -at amber -rn NLE
```

RESP stage 1

固定主链的四个原子的电荷与AMBER FF19SB保持一致

```
#NLE.ac
ATOM      3  N1  NLE     1       1.695  -0.237  -0.888 -0.555324          N
ATOM     16  H4  NLE     1       2.118  -0.202  -1.801  0.338581          H
ATOM      5  C4  NLE     1       0.303   1.695  -0.036  0.619448          C
ATOM      7  O1  NLE     1      -0.112   2.693  -0.600 -0.557903          O

```

```
#AMBER FF19SB种对应的参数
70          N       4    TYR       N      70 -0.41570000  14.010000   ; qtot 1.584301
71          H       4    TYR       H      71 0.27190000   1.008000    ; qtot 1.856201
89          C       4    TYR       C      89 0.59730000  12.010000    ; qtot 2.567901
90          O       4    TYR       O      90 -0.56790000  16.000000    ; qtot 2.000001
```

固定封端部分的原子参数与AMBER FF19SB保持一致

```
aminoct12.lib
!entry.NHE.unit.atoms table  str name  str type  int typex  int resx  int flags  int seq  int elmnt  dbl chg
 "N" "N" 0 1 131072 1 7 -0.463000
 "HN1" "H" 0 1 131072 2 1 0.231500
 "HN2" "H" 0 1 131072 3 1 0.231500
```

```
aminont12.lib
!entry.ACE.unit.atoms table  str name  str type  int typex  int resx  int flags  int seq  int elmnt  dbl chg
 "H1" "HC" 0 1 131072 1 1 0.112300
 "CH3" "CT" 0 1 131072 2 6 -0.366200
 "H2" "HC" 0 1 131072 3 1 0.112300
 "H3" "HC" 0 1 131072 4 1 0.112300
 "C" "C" 0 1 131072 5 6 0.597200
 "O" "O" 0 1 131072 6 8 -0.567900
```

限制CH2和CH3的H带相同的电荷

methyl and methylene groups

修改ANTECHAMBER_RESP1.IN

参考手册：RESP (lu.se)

根据以上需求，重点设置和修改的参数

ihfree = 1, hydrogen atoms are not restrained

ioutopt = 1,

iqopt = 2, read initial charges from -q

-1 表示fixed initial charges

Valid fitting_numbers are:
-n fixed charge (to the one in file qin)
0 free charge
n the charge is constrained to be the same as the one of atom #n.

The keywords mean:
ihfree (0 = hydrogen atoms are restrained; 1 = not restrained)
qwt (wheight of the constraint. Use 0.0005 for stage 1 and 0.0001 for stage 2)
iqopt (1 = set all initial charges to 0; 2 = read initial charges from -q (qin)
irstrnt (0 = harmonic restraints; 1 = hyperbolic restraints, default)
nmol (number of molecules, i.e. different conformations)

```
Resp charges for organic molecule

 &cntrl

 nmol = 1,
 ihfree = 1,
 ioutopt = 1,
 iqopt = 2,
 qwt = 0.00050,

 &end
    1.0
Resp charges for organic molecule
    0   28
    6   -1
    6   -1
    7   -1
    6    0
    6   -1
    7   -1
    8   -1
    8   -1
```

```
    6    0
    6    0
    6    0
    6    0
    1   -1
    1   -1
    1   -1
    1   -1
    1    0
    1   -1
    1   -1
    1    0
    1   20
    1    0
    1   22
    1    0
    1   24
    1    0
    1   26
    1   26

```

修改qin

qin中需要重点关注需要固定的电荷信息

```
-0.366200  0.597200 -0.415700  0.032317  0.597300 -0.463000 -0.567900 -0.567200
 0.076693 -0.239859  0.096580 -0.229204  0.112300  0.112300  0.112300  0.271900
 0.016668  0.231500  0.231500  0.031084  0.031084  0.074657  0.074657 -0.001422
-0.001422  0.060622  0.060622  0.060622
```

提交RESP任务

```
resp -O -i ANTECHAMBER_RESP1.IN -o resp.out1 -q qin -e ANTECHAMBER.ESP
```

RESP stage 2

qwt (wheight of the constraint. Use 0.0005 for stage 1 and 0.0001 for stage 2)

限制信息与RESP stage 1相同

对RESP进行两次拟合（对比两次拟合的区别和联系，是对哪些地方进行了优化？）

stage 1: qwt = 0.0005

stage 2: qwt = 0.0001

```
cp qout qin2
resp -O -i ANTECHAMBER_RESP2.IN -o resp.out2 -q qin2 -e ANTECHAMBER.ESP
```

prepgen拟合

准备NLE.mc文件

```
#NLE.mc
HEAD_NAME N1
TAIL_NAME C4
MAIN_CHAIN C3
OMIT_NAME C2
OMIT_NAME O2
OMIT_NAME C1
OMIT_NAME H1
OMIT_NAME H2
OMIT_NAME H3
OMIT_NAME N2
OMIT_NAME H6
OMIT_NAME H7
PRE_HEAD_TYPE C
POST_TAIL_TYPE N
CHARGE 0
```

生成NLE.prepin

```
prepgen -i NLE.ac -o NLE.prepin -m Nle.mc -rn NLE
```

注意事项：

修改原子名称和原子类型

使用配套力场的参数，比如amber ff19SB, 对应**parm19.dat，将主链原子的编号和顺序与标准氨基酸更改一致，方便后续对轨迹进行分析**

合并拟合后的RESP参数

按照原子名称逐个进行对应！

由于最后的总电荷为-0.0007，因此对七个H原子各+0.0001，最后总RESP电荷为0

生成frcmod参数

```
parmchk2 -i NLE.prepin -f prepi -o frcmod.NLE -a Y -p parm19.dat
```

与标准力场进行比较

可以通过tleap模块中的savemol2来输出RESP信息

mol2中可以保存4位有效数字，pdb只能保存2位有效数字

test.mol2

8.96KB